*smith&nephew

**REFLECTION◊ Ceramic Acetabular System**

**Important Medical Information**

**Warnings and Precautions**

## DEVICE DESCRIPTION

The REFLECTION Ceramic Acetabular System is a ceramic-on-ceramic hip prosthesis composed of modular components that include the REFLECTION ROUGHCOAT™ porous coated acetabular shell, alumina ceramic acetabular shell liner, and an alumina ceramic femoral head. All implantable devices are for single use.

Acetabular Shell/Cup

Acetabular shells are manufactured from Ti-6Al-4V (ASTM F 1472 and ISO 5832/3). There are eleven sizes of acetabular shells available, ranging from 46 mm through 66 mm outer diameter in 2 mm increments. Each shell features an apex hole to accept the cup positioner / impactor instrument. Shells have five additional holes arranged about the apex hole. These holes are for optional, adjunctive screw fixation to the superior acetabulum. Universal cancellous screws in a 6.5 mm diameter are available in lengths of 15 to 50 mm in 5 mm increments. Screws are self-tapping, but the screw holes in the acetabulum need to be pre-drilled to the minor diameter of the screw. Hole covers are available to cover the shell holes if desired. Screws and hole covers are manufactured from Ti-6Al-4V ELI (ASTM F 136). The shell's internal geometry is a Morse taper that locks the ceramic liner when inserted. The outer shell geometry is hemispherical and ROUGHCOAT porous coated with commercially pure titanium (ASTM F 67 and ISO 5832/2). The porous coating encompasses the entire outer surface of the shell except for a small one millimeter strip around the edge of the rim. The shell has a flat rim with no build-up or recessed features until the rim meets the inner taper. At that location, the rim features an approximately 1 mm bevel around the circumference. The rim surface has six small depressions equally spaced around the circumference. These shallow depressions allow the liner extraction tool prongs to be used for ceramic liner removal when necessary.

Acetabular Liner/Insert

The alumina ceramic acetabular liners are manufactured from BIOLOX™ forte Aluminum Oxide (ASTM F 603 and ISO 6474) and are available in five sizes. The shell's outer diameter size and the corresponding femoral head diameter limit the choice of acetabular liner used with an acetabular shell. Three, 28 mm internal diameter liners are available for use with the acetabular shells. One size liner(28/37G)fits 46-48 mm O.D. shells, one size (28/41G) liner fits 50-54 mm O.D. shells, and one size (28/44G) liner fits 56-66 mm O.D. shells. Two, 32 mm internal diameter liners are available for use with the acetabular shells. One size liner (32/41G) fits 50-54 mm O.D. shells, and one size (32/44G) liner fits the 56-66 mm O.D. shells.

Femoral Head

The alumina ceramic ball heads are manufactured from BIOLOX forte Aluminum Oxide (ASTM F 603 and ISO 6474). The alumina ceramic ball heads are available in six sizes: three heads with an outer diameter of 28 mm and three heads with an outer diameter of 32 mm. Each

diameter head size has three different neck lengths, short (+0), medium (+4), and long (+8) for proper anatomic and musculature fit. Externally, all ball heads are highly polished. All ball heads have an internal bore taper angle of 5° 46' for high conformity with the 12/14 cone taper of the femoral stems. The alumina ceramic heads lock onto the machined taper and do not rotate on the stem.

The REFLECTION Ceramic Acetabular System is suitable for use with the 12/14 taper of Smith & Nephew's commercially available titanium alloy, cementless Synergy femoral stems or cobalt chromium alloy cemented Spectron EF stems both available in standard and High Offset versions.

## INDICATIONS FOR USE

The REFLECTION Ceramic Acetabular System is indicated for use in patients requiring primary total hip arthroplasty due to non-inflammatory arthritis (degenerative joint disease) such as osteoarthritis, avascular necrosis, or traumatic arthritis.

## CONTRAINDICATIONS

The REFLECTION Ceramic Acetabular System is contraindicated in individuals exhibiting any of the following:

- Insufficient quantity or quality of bone support; metabolic bone disease; osteoporosis
- Neurological or muscular conditions that would place extreme load or instability upon the hip joint
- Active joint infections or chronic systemic infection
- Obese patients where obesity is defined as three times normal body weight
- Skeletal immaturity

## WARNINGS and PRECAUTIONS

Improper selection, placement, positioning, and fixation of the implant components may result in unusual stress conditions and subsequent early failure/fracture of the components. The surgeon should be thoroughly familiar with the implants, instruments, and surgical procedure prior to performing surgery. Certain insertion techniques may be different than those known for conventional hip systems, and are specifically designed to avoid potential implant failures.

PREOPERATIVE

- The patient should be warned of the brittle nature of the ceramic components and the possibility of failure the device leading to additional surgery in the future. The patient should be warned that the implant can break or become damaged as a result of strenuous activity or trauma including extreme activity or heavy labor for occupation or recreation.

- Do not implant in pregnant patients as the extra weight and exposure to radiation may be harmful to the implant and baby, respectively.

- Do not substitute another manufacturer's device for any of the REFLECTION Ceramic Acetabular System components because design, material, or tolerance differences may lead to premature device and/or functional failure. Components have been specifically designed to work together. (see product literature for list of appropriate components).

- Use extreme caution in storage and handling of ceramic components during assembly because of the brittle nature of ceramic material. Cutting, bending, or scratching the surface or taper area of components can alter the mechanical characteristics of the implant system leading to failure. Do not allow the porous coating surfaces to encounter cloth or fiber-releasing material as cloth fibers may interfere with implant stability leading to early failure of the implants.

- Carefully examine each ceramic component for any signs of damage that may have occurred during shipping or prior in-hospital handling. All surfaces should be smooth without pitting, scratches, or other surface irregularities. Do not implant any damaged components.

- Specialized instruments are available and must be used to assure the accurate implantation of prosthetic components. Examine instruments for wear or damage prior to surgery. Instruments that have experienced extensive use or excessive force are susceptible to fracture and must not be used.

- Do not resterilize REFLECTION Ceramic Acetabular System Implants i.e. alumina ceramic heads, liners or porous coated metal implants as they require special cleaning instructions and are to be returned to the manufacturer (see Sterilization section below).

- Do not implant this hip system in patients undergoing revision of previously unsuccessful femoral head replacement, cup arthroplasty, or other indications (e.g. inflammatory hip joint disease) because the safety and effectiveness of these devices for indications other than non-inflammatory degenerative joint disease have not been established.

INTRAOPERATIVE

- Implants are for single use only. Never reuse an implant component as internal stresses that are not visible may lead to early failure of these components. If broken ceramic material is encountered intraoperatively or postoperatively, remove all loose identifiable fragments, and thoroughly irrigate and suction the operative site.

- **Replace both the ceramic insert and the metal acetabular shell (refer to specific procedure in Surgical Technique manual) if the insert is chipped, cracked, or otherwise damaged during the implant procedure or postoperative timeframe.** Once the acetabular shell taper has been deformed through assembly to its mating ceramic insert, it should not be reassembled to another ceramic insert. Return the broken fragment(s) to Smith & Nephew for evaluation.

- The ceramic liner and ceramic head should not be implanted if the liner or head is damaged (e.g., if damaged as a result of the shipping process, if dropped on the floor, or if scratched by an instrument) or if cone of the stem is damaged as this can significantly affect the structural integrity of the components.

- Do not reassemble and disassemble the ceramic head and metal femoral stem or a liner component to the acetabular shell because the locking joint and taper joint may become damaged.

- Ensure appropriate type and size components selected correspond with anatomical and biomechanical factors such as patient age and activity levels, weight, bone and muscle conditions, any prior surgery. Generally, the largest cross-section component that will allow adequate bone support to be maintained is preferred. Failure to use the optimum-sized component may result in loosening, subluxation, dislocation, bending or fracture of the component and/or bone.

- Ensure appropriate selection of the Universal Cancellous Bone Screw length and location if adjunctive fixation of the acetabular shell is to be used. Do not place a screw in the center (apex) hole of the acetabular shell. Bone screws must be completely seated in the shell holes to allow proper locking of the ceramic liner. Do not use pegs in the shell holes.

- Do not cut, bend or scratch the surface or taper area of components as this can significantly alter the mechanical characteristics of the implant system causing failure under load.

- Do not use a metal or zirconia head with the REFLECTION Ceramic Acetabular System because this may accelerate bearing wear and lead to early failure of the device.

- Clean surgical debris (including bone cement) and dry all shell taper and stem taper surfaces prior to seating and impacting the ceramic components. Do not allow the porous surfaces to encounter cloth or fiber-releasing material. Debris may inhibit the component locking mechanism leading to early failure of the implants.

- Ensure that prior to liner insertion, soft tissue does not interfere with the shell/liner interface. Modular components must be assembled securely to prevent disassociation.

- Always ensure proper alignment and seating of the trial insert before seating the actual insert. Subtle mal-alignment may not be immediately obvious and can result in liner failures (chipping/cracking/splitting) during impacting. Range of motion should be thoroughly checked for impingement or instability with the trial insert. If ROM is unsatisfactory, component repositioning should be performed unless attributable to obvious causes that can be corrected (e.g., presence of osteophytes, bony protrusions, or other movement limiting features).

- Seat the insert gently by hand into the shell before impacting (with plastic impactor head placed on the shell positioner/impactor) to prevent chipping or damage. **Repeated impaction of the liner in the shell when the initial attempt at seating the liner is unsuccessful is not recommended and may lead to early failure.**

- Ensure correct selection of the head neck length, cup and stem. Increased neck length and varus positioning will increase stresses that must be borne by the stem. Suggested seating of acetabular shell is a 45° inclination with 15° anteversion for proper positioning to decrease the chance for dislocation. **If the ceramic liner and shell are not fully seated or are aligned incorrectly after final impaction, it will be necessary to revise the shell and liner with new components.**

POSTOPERATIVE

- Strict adherence to the postoperative weight bearing and activity protocol is needed to protect the implant from failure until adequate fixation and healing have occurred. Excessive activity and trauma affecting the joint replacement have been implicated with premature failure.
- Extreme care in patient handling (moving patient, placing on bedpans, changing clothes, etc.) immediately after surgery is necessary. Adequate support should be provided to the operative leg when moving the patient to avoid placing excessive load on the operative leg.
- The patient should be advised to report any pain, decrease in range of motion, swelling, fever, squeaking or clicking noises and unusual incidences. Patient reports of squeaking or clicking should be carefully evaluated as they may indicate position changes in the components compromising the durability of the implants.
- The patient should be cautioned to monitor activities and protect the replaced joint from unreasonable stresses, and follow the instructions of the physician with respect to follow-up care and treatment. In particular, the patient should be warned against unassisted activity, particular use of toilet facilities and other activities requiring excessive motion of the hip.
- Periodic x-rays are recommended to detect long-term evidence of changes in position, loosening, bending and/or cracking of components or bone loss. Should there be evidence of loosening, bending and/or cracking of components or bone loss; patients are to be closely observed with the possibilities of further deterioration evaluated, and the benefits of early revision considered. If the ceramic head must be revised for any reason and the hip stem is firmly fixed, the revision should be made with a CoCr head and corresponding polyethylene liner and metal shell.

## POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential Complications Associated with Any Total Hip Arthroplasty surgery

- excessive wear of the implant components secondary to impingement of components or damage of articular surfaces
- fracture, migration, loosening, subluxation, or dislocation of the prosthesis or any of its components; any of which may require a second surgical intervention or revision;
- intractable pain
- unintended bone fractures
- metal sensitivity reactions or other allergic/histological reactions to implant material
- vascular damage resulting in large blood loss, or
- neurologic injury resulting in transient or permanent functional and/or sensory deficits
- leg length change/discrepancy
- deep venous thrombosis
- pulmonary or vascular embolism
- superficial or deep infection, delayed wound healing
- periarticular calcification



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- myocardial infarction
- Gastrointestinal complications
- Genitourinary complications
- Decreased range of motion
- Aggravation of other joint or back conditions (due to positioning during surgery, postoperative leg length discrepancy, muscular deficiencies, etc.)
- death

Potential Complications Associated with Ceramic on Ceramic Hip Systems

Due to the materials of the device, these may include, but are not limited to, femoral head breakage, acetabular insert (liner) fracture, component dissociation dislocation and component wear debris. Other adverse events, common to other hip systems may also occur but at different frequencies.

## SUMMARY OF CLINICAL TESTING

A multicenter, prospective, open-label concurrently controlled clinical trial comparing outcomes for patients randomized to either REFLECTION Ceramic Acetabular System (C/C) or the REFLECTION alumina ceramic-on-polyethylene system (C/P) as a control was conducted at 10 investigational centers by 14 investigating surgeons. The study was designed as non-inferiority trial with a 10% non-inferiority margin to evaluate the safety and effectiveness of the REFLECTION Ceramic Acetabular System (i.e., the success rate in the REFLECTION Ceramic Acetabular System group is not worse than the success rate in the active control group by more than 10%.)

Three diagnostic indications were eligible for randomized enrollment: 1) non-inflammatory arthritis (RNIA) 2) inflammatory arthritis (RIA) or 3) revision of failed implant (RR). Subsequent to completion of enrollment limit in the non-inflammatory arthritis diagnostic indication, additional subjects were enrolled in a non-randomized manner under 'Continued Access' at the same investigational centers (CAC). Device effectiveness was assessed by comparison of preoperative and postoperative changes in hip pain, function, and range of motion as measured by Harris Hip Score (HHS) tool. Pain appraisal involved the patient's current assessment of the affected hip discomfort level. Functional parameters include gait assessment of limp, support required to walk, and distance able to walk, activity assessments of ability to use stairs, put on shoes and socks, sitting, and access transportation. Range of motion measurements included flexion, abduction, adduction, and internal and external rotation movements. Device safety was assessed by analysis of all adverse events experienced by patients in each treatment group. Pre-defined criteria were compared to determine overall success between groups

### A. Study Design

Pre-defined inclusion/exclusion criteria were identified in the investigational plan. Patient randomization occurred prior to surgery, using a 1:1 randomization scheme whereby a patient (hip) was to receive either a ceramic-ceramic articulation (C/C) construct or a ceramic-polyethylene articulation (C/P) construct. Bilateral hip arthroplasty patients were randomized only once with the contralateral hip receiving the same treatment as the first hip was randomized to receive, except in one case. For each diagnostic indication group, randomization was stratified by investigational center with a fixed block size of 2. Sequentially



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numbered envelopes containing the randomized treatment assignment were prepared and distributed to each center. The patients and investigators were not masked to the hip system received. All x-ray films were reviewed by an independent radiologist who was not specifically advised as to treatment group prior to, or during the review. Each hip was assessed separately and followed up according to its own evaluation schedule. Patients were evaluated preoperatively to establish demographics and baseline effectiveness measurements; then intraoperatively, at discharge from the hospital, and at 3, 6, 12, and 24 months postoperatively using surrogate endpoints of pain, function, quality of life, radiographic parameters and the occurrence of adverse events to demonstrate safety and effectiveness. Patients were evaluated biennially thereafter until all patients had reached their 24 months evaluation.

## 1. Inclusion and Exclusion Criteria

Inclusion Criteria

Patients meeting all of the following inclusion criteria were enrolled in the study:

- Primary diagnosis of osteoarthritis, rheumatoid, or revision
- Males or females, 21-80 years old
- Able to follow-up for 2 years
- HHS $\leq$ 60
- Preoperative medical clearance; free or treated for cardiac, pulmonary, hematological conditions that pose excessive operative risk
- Meets no exclusion criteria

Exclusion Criteria

Patients who met one of the exclusion criteria were not eligible for enrollment in the study:

- Morbid Obesity $\geq$ 100 pounds over desirable body weight
- Insufficient bone from cancer, femoral osteotomy, Girdlestone, osteoporosis, metabolic disorders
- Charcot joint, muscle deficiencies, multiple joint disabilities
- Active localized or systemic infection
- Skeletal immaturity
- Psychological illness, mental illness, mental retardation, or drug, alcohol abuse
- Pregnancy
- Immunosuppressive disorder: corticosteroid use*, cytotoxic drugs, antilymphocytic serum, irradiation, AIDS, immunosuppressive therapy, auto immune diseases (except rheumatoid arthritis). * Patients using 0.1 to 80 mg/day were not excluded in this study.
- Subject participating in any other pharmaceutical, biologic, or medical device clinical investigation
- Known sensitivity to the materials in the device

## 2. Clinical Assessment

Clinical patient evaluations were performed preoperatively, intraoperatively, and at discharge. Evaluations were also performed postoperative at 3 months, 6 months, 12 months, and 24 months and biennially thereafter for any applicable patients. Preoperatively, patient demographics and basic medical history was collected. Patient outcomes were evaluated for the involved hip using a modified Harris Hip Score Scale* a rating scale that incorporates subsections relating to hip pain; functional gait and activities of daily living; deformity and range of motion. The Harris Hip Score scale scoring ranges from 0 (worst) to 100 (best). A modified Harris Hip Score was used, which allowed simpler calculation of range of motion results. A patient self-assessment (SF-12) general health survey was administered to collect quality of life outcome information also. Intraoperatively, information was collected that consisted of the surgical technique performed, any intraoperative or perioperative complications/adverse events which may have occurred and any other relevant implant-related information needed to characterize the performance of the device. At discharge, patients were assessed for ambulatory status and incidence of adverse events since surgery. Discharge x-rays served as the baseline radiographic assessment for later comparisons. A/P and Lateral radiographs were assessed for implant position and evidence of radiolucencies. Clinical evaluations were standard at each postoperative interval. Each postoperative visit consisted of a Harris Hip Score evaluation, radiographic assessment and SF-12 Health Survey. Any adverse event occurring since the previous visit evaluation interval was recorded. At some early intervals (3 months), collection of radiographs and SF-12 surveys were optional. Site investigators were responsible for assessing patients at all intervals. For the 24 month interval, radiographs were also independently evaluated by a radiologist.

## 3. Success Criteria

The primary endpoint of the clinical trial was an overall patient success outcome determination at 24 months, which included a composite of implant survivorship, Harris Hip Score, and radiographic evaluation. A successful patient at 24 months met all of the following required criteria:

- no revision of any device system component through the two years evaluation;
- a total Harris Hip Score greater than or equal to 80 (excellent to good score); and
- no evidence of unacceptable radiolucencies or position change along the cup and stem (radiographic failure) as defined by exhibiting radiolucencies of:
  a. greater than 50% of the total bone prosthesis interface; and/or
  b. greater than or equal to 2 millimeters in two or more zones; or
  c. if the patient has subsidence of the femoral stem or migration of the acetabular prosthesis of greater than 5 millimeters with associated clinical findings.

* Canale, T., editor. Campbell's Operative Orthopaedics. St. Louis:Mosby, Inc.; 2003.

The success criteria were used to assess the overall treatment success for the study device versus control device populations. Patients (hips) were categorized as a success or non-success, and the comparison between the two treatment groups is indicative of the devices performance in the study populations.

**4. Statistical Analysis**

The randomized non-inflammatory arthritis cohort (RNIA) represented over 80% of the total hip replacements performed in the study; therefore, any statistical testing between device groups were only performed for this cohort at the 2-year visit. For the other two diagnostic groups, only descriptive statistics were generally provided.

The safety and effectiveness of the REFLECTION Ceramic Acetabular System was assessed by analyzing the Patient Success Criteria, which include revision status, functional/clinical evaluation, and radiographic assessments. A non-inferiority hypothesis was used to test the difference in the probability of patient's success with a 10% margin. The null hypothesis was the success outcome rate at 2 years in the control group is greater than the success rate in the study device group by at least 10%, and the alternative hypothesis is that the difference in success rates between the two groups is less than 10%. The null hypothesis will be rejected if the upper bound of the two-sided 90% confidence interval (CI) for the difference in success rates is less than 10% and conclude that the study device is non-inferior to the control. A logistic regression model and GEE model for the success outcome at 2 years were also performed to evaluate the effect of device group, body mass index, age, gender, type of hip replacement (unilateral vs bilateral), femoral stem cement use (yes vs no) and investigational site.

Additionally, the risk of ceramic-ceramic articulation was assessed by analyzing the revision rate by two years, applicable operative and postoperative adverse events (device related or otherwise); Survivorship analysis was assessed using Kaplan-Meier methodology.

Results on hip pain, function, and range of motion were also compared between the study and control groups using Wilcoxon rank sum test. The incidence of radiographic failures were compared between the two groups using Fisher's Exact Test. Fisher's Exact Test was also used to compare the percentage of patients reporting each type of adverse event between the two device groups. Multiple occurrences of the same event reported by the same patients were counted as only once. Results from SF-12 health survey at 2 years were compared using a two-sample t-test.

**B. Study Population/Demographics**

In total, 399 patients were implanted with 460 devices in the investigational study under the study protocol at 10 investigational sites by 14 investigating surgeons. One patient was counted twice as the patient had one of each device implanted in each of his hips. In the randomized non-inflammatory arthritis (RNIA) study cohort, there were 146 patients who received the investigational device and 130 patients who received the control device at 10 investigational sites. In the inflammatory arthritis cohort, there were 14 patients at 7 investigational sites who

received the investigational device. In the revision cohort, 5 patients received the investigational device at 4 sites. All patient cohorts were evaluated in the safety analysis. Effectiveness was based on only the RNIA cohort.

For all RNIA subjects enrolled, males accounted for 114/174 (65.5%) and 84/141 (59.2%) in the study and control groups, respectively; and the mean body mass index was 28.9 and 28.1 kg/m$^2$ in the study and control groups, respectively. The mean age at surgery as determined from a patient analysis was 50 years and 54.3 years in the study and control groups, respectively; and difference in average age between the two groups is significantly different (p-value 0.0121, Wilcoxon rank sum test). The two treatment groups were very similar demographically, and there were no statistically significant ($p < 0.05$) differences for any of the other variables. Ethnic demographic data was not collected. There was a predominance of male patients; younger patients and more bilateral patients were enrolled in the investigational group. The demographics of the randomized non-inflammatory arthritis cohort as determined from an all Hip analysis is detailed in Table 1.

**Table 1, Demographics – All Hips**

| Description of the Study Populations | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Non-Inflammatory RNIA | | Inflammatory RIA | | Revision RR | | Continued Access CAC |
| | C-C | C-P | C-C | C-P | C-C | C-P | C-C |
| Number of hips/ (patients)* | 174 (146) | 141 (130) | 17 (14) | 13 (10) | 5(5) | 7(7) | 103 (88) |
| Bilateral hips (%) | 57 (33%) | 23 (16%) | 6 (35%) | 6 (46%) | 0 | 0 | 30 (29%) |
| Men / Women | 114/60 | 84/57 | 10/7 | 4/9 | 3/2 | 4/3 | 60/43 |
| Age, year (mean) | 50 | 53.9 | 47.6 | 44.3 | 50 | 62.7 | 46.2 |
| Age < 40 | 23.5% | 11.5% | | | | | |
| 40 ≤ Age ≤ 69 | 70.3% | 74.6% | | | | | |
| Age > 69 | 6.2% | 13.9% | | | | | |
| Height (cm) | 173.9 | 172.7 | 166.1 | 169 | 174.8 | 170 | 173.1 |
| Weight (Kg) | 87.6 | 84.3 | 77.8 | 78.3 | 89.2 | 77.4 | 86.3 |
| BMI (kg/m$^2$) | 28.8 | 28.1 | 28.5 | 27.4 | 29.4 | 26.9 | 28.7 |
| Previous surgery on Affected hip | | | | | | | |
| YES | 33 | 23 | 2 | 0 | 5 | 7 | 21 |
| NO | 141 | 118 | 15 | 13 | 0 | 0 | 82 |
| Other joint involvement: YES | 107 | 83 | 14 | 10 | 3 | 4 | 47 |
| NO | 67 | 58 | 3 | 3 | 2 | 3 | 56 |
| Physical Activity | | | | | | | |
| None | 12 | 4 | 0 | 0 | 2 | 1 | 7 |
| Light | 107 | 94 | 13 | 12 | 3 | 5 | 66 |
| Moderate | 50 | 37 | 4 | 1 | 0 | 0 | 27 |
| Intense | 5 | 6 | 0 | 0 | 0 | 0 | 3 |

*one patient was counted twice because the patient had one of each device implanted in each of his hips

## C. Hip/Patient Accountability

Accountability of numbers of hip and patients analyzed is shown in Table 2 below for the RNIA cohort as this is the primary study group. Note that eighteen ceramic-ceramic hips and twenty-five ceramic-poly hips were identified as either minor or major protocol deviations, and these hips are excluded from the efficacy analysis.

This resulted in 156 ceramic-ceramic hips and 116 ceramic-poly hips analyzed for effectiveness in the RNIA cohort at 2 years.

Discontinued Patients

At the 2 years evaluation interval there were 86 hips, that were discontinued during the course of the study (70 hips in the RNIA, 9 hips in the RIA, 7 hips RR). Discontinued refers to hips that did not have clinical follow-up at two years due to any reason, i.e. lost to follow-up, dead, revised, not yet due for follow-up at 2 years, etc.

**Table 2, Hip Procedure Follow-up Accountability – Per Protocol RNIA Cohort**

| | Preop | | 3-months | | 6-months | | 1-year | | 2-years | | 2+ years | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Category** | **C/C** | **C/P** | **C/C** | **C/P** | **C/C** | **C/P** | **C/C** | **C/P** | **C/C** | **C/P** | **C/C** | **C/P** |
| **Theoretically Due**[1] | 156 | 116 | 156 | 116 | 155 | 116 | 154 | 116 | 150 | 116 | 150 | 116 |
| **Deaths** * | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 0 |
| **Revisions** | 0 | 0 | 2 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 2 | 0 |
| **Expected**[2] | 156 | 116 | 153 | 115 | 151 | 115 | 150 | 115 | 145 | 114 | 145 | 114 |
| **Evaluated**[3] | 156 | 116 | 142 | 104 | 137 | 99 | 128 | 94 | 126 | 85 | 128 | 85 |
| **Actual % Follow-Up** | 100% | 100% | 92.8% | 90.4% | 90.7% | 86.1% | 85.3% | 81.7% | 86.9% | 74.6% | 88.3% | 74.6% |

C/C = ceramic-ceramic; C/P = ceramic-polyethylene

Note: Modified per protocol analysis excludes all major and minor deviations from the investigational plan (C/C: 174-18 protocol deviations = 156, C/P: 141-25 protocol deviations = 116)

[1] Theoretically due is the number due at each interval based on the date of surgery and date of database closure.

[2] Expected is the number theoretically due minus cumulative deaths and revisions.

[3] Evaluated is actual Total Harris Hip Score or Function Score obtained but the number excludes evaluations on previously revised hips.

* Deaths post-revision are not subtracted from Theoretically Due to achieve Expected. 2 patients (hips) died after revision. In C/C group, there are 7 cumulative deaths and revisions through 2 years, and thus only 5 hips are subtracted from Theoretically Due at 2 years.

At the completion of the study there had been four deaths in the RNIA investigational group and one in the control group. No other deaths occurred in any of the other cohorts or in the Continued Access cohort. Revision surgery was performed in 6/156 (3.9%) RNIA hips in the investigational and 2/116 (1.7 %) hips in the control group. One revised RNIA C/P hip was a protocol deviation that is not reflected in the per protocol accounting of Table 2. Revisions occurred in 1/17(5.9%) of hips in the RIA cohort, 0/5 (0%) of the hips in the Revision cohort, and 5/103 (4.8%) of the hips by one year in the CAC cohort. There were no revisions in the control groups of the RIA or Revision cohorts. At 24 months, 126 hips were evaluated in the RNIA investigational group and 85 hips were evaluated in the control group. Since the overall success criteria was based on a three part composite of revision status, clinical function, and radiographic results at two years, some hips may be evaluated at two years but still be missing one or more components of the three components. However, at two years, there were 122 hips in the ceramic-ceramic group and 81 hips in the ceramic-poly group with all three components necessary to evaluate success. At the time of data base closure no patients in the continued access cohort had reached the 24 month evaluation interval.

## D. Study Period

The first patient was implanted in November of 1998. All patients in the randomized non-inflammatory arthritis cohort had reached their 24 month postoperative period as of the data base closure on February 24, 2003. However, the second hip replacement in 7 investigational device patients was not yet due at 2 years follow-up. With 2 year follow-up required on all patients, the total duration of this study was 4.25 years. A change to the device was made on April 17, 2001, which redesigned the accepting shell/cup to have a chamfered edge in an attempt to reduce the potential cracking, chipping, fracture or other damage to the ceramic liner upon insertion. This design change would not have significant impact on the results of the clinical trial.

## E. Safety and Effectiveness Data

### 1. Safety Data

Safety was determined through the comparison of adverse event rates both device related and unrelated, implant survival, and radiographic analyses for all patients, randomized or non-randomized, receiving the device. In the total enrolled population, there were 4 intraoperative revisions due to liner chipping upon insertion, and 12 postoperative revisions in 299 hips implanted (for any indication and including the Continued Access hips – see Table 1) with the ceramic on ceramic hip system. One intraoperative revision due to instability and 2 postoperative revisions in 161 hips occurred with the control device.

The rate of specific adverse events, particularly, revisions, HO, dislocation, and proximal linear femur fractures were higher in the investigational group for all hips in the RNIA cohort.

Revisions

In the RNIA cohort, six postoperative revisions in 174 hips (3.4%) occurred in the C/C group. Two hips revised at three months due to dislocation in one hip and infection in the other case. One hip was revised at six months due to recurrent dislocations. At two years or greater, revisions were required for one hip with a fractured ceramic femoral head, one hip with a fractured ceramic acetabular liner, and one hip with a loose femoral component. Two postoperative revisions in 141 hips (1.4%) occurred in the C/P RNIA group. Revision was required in the discharge period for one hip due to instability, and one hip at three months due to an infection (Table 3). The estimate of the proportion of hips without revision at two years, in the RNIA cohort was 98% (95% CI: 95%-100%) for the C/C group and 99% (97%-100%) for the C/P group. The revision free-survival was not statistically significantly different between the two groups (Log- rank test, p=0.3438).

In the Continued Access population of 103 hips, five hips (4.9%) were revised by 1 year. One hip was revised at 3 months for prolonged dislocation. Two hips were revised at 6 months (one hip for dislocation and one hip for loose stem). At

one year or more, two hips were revised due to one infected hip and one case of osteolysis. One ceramic-ceramic hip in the RIA cohort was revised at 6 months due to stem subsidence. There were four hips revised intraoperatively due to liner chipping during insertion that required immediate cup/liner exchange.

The revision rate for this study to date is 16/299 (5.4%) hips (see Table 1) with revisions in the C/C group at all evaluation intervals for all cohorts. The rate for the RNIA Cohort C/C group is 8/134 = 6% (174 – 40 hip exclusions) and is 8/174 = 4.6% without hip exclusions. The rate for the RNIA Cohort for the C/P control group is 3/102 =3% (141 – 39 hip exclusions) and is 3/141=2.1% without hip exclusions. The rate for the non-inflammatory Continued Access cohort is 7/103 =6.8% at 1.5 years, with incomplete follow-up at 2 years (1 hip with a revision at 2 year window included).

**Table 3, Revised Hips – RNIA Cohort**

| Treatment | Interval | Reason for Revision | Components Revised |
|---|---|---|---|
| C/C | Intraop | Chipped liner | cup, liner |
| C/C | Intraop | Chipped liner | cup, liner |
| C/C | 3 month | Dislocation | liner, head |
| C/C | 3 month | Infection | All components |
| C/C | 6 month | recurrent anterior dislocations | cup, liner, head |
| C/C | 2 year | Ceramic head fracture | liner, head |
| C/C | Post 2 year | Ceramic liner fracture | cup, liner, head |
| C/C | Post 2 year | loose femoral component | head, stem |
| C/P | Intraop | Instability | Liner |
| C/P | Discharge | Instability | liner, head |
| C/P | 3 months | Infection | All components |

C/C=ceramic-ceramic; C/P=ceramic/polyethylene

Heterotopic Ossification

The overall incidence of heterotopic ossification was found as follows in Table 4 for the RNIA Cohort.

**Table 4, Incidence of Hips with HO- RNIA Cohort**

| HO * | C/C (N=174) | C/P (N=141) |
|---|---|---|
| Grade I | 36 (20.7%) | 31 (22%) |
| Grade II | 7 (4%) | 3 (2.1%) |
| Grade III | 7 (4%) | 2 (1.4%) |
| Grade IV | 1 (0.6%) | 0 (0%) |

* Brooker Classification

Dislocations

There were 25 dislocations reported for this study for all cohorts at all intervals. Of these, 11 events (4 intraoperative and 7 postoperative) occurred in 7 hips in those patients randomized to the ceramic-poly group. In the ceramic-ceramic group, there were 14 postoperative dislocation events in 9 hips. A majority of the dislocations (7 hips /10 events) in the ceramic-ceramic hips occurred in the first 3 months.

Proximal linear femur fractures

These events occurred intraoperatively in 7 ceramic-ceramic hips, 4 in the control group and 3 in the continued access group. All fractures occurred during preparation of the femoral canal or during actual stem insertion.

Adverse Events by time of occurrence

Within the RNIA cohort, there were a total of 34 intraoperative Operative Site adverse events that were seen in 17/174 hips (9.8%) that received the REFLECTION Ceramic Acetabular device and 8/141 hips (5.7%) in the control group. The intraoperative, Operative Site adverse events that occurred most frequently in the ceramic-ceramic group were proximal medial linear split (bone) fracture in 7/174 hips (4.0%), blood loss greater than 1500 ml in 6/174 hips (3.4%) and difficulty implanting the alumina ceramic acetabular liner in 2/174 hips (1.1%). Other events reported once (1/174=0.6%) were insufficient bone stock, nerve injury, and trochanteric fracture. The rate of events was comparable to the control group with the exception of difficulty implanting a ceramic liner.

In the RNIA cohort, 117 postoperative Operative Site Adverse Events were reported in 62 hips in the C/C study group, as compared to 72 events in 45 hips in the C/P group. The postoperative complications involving HO Grades I, II, and/or II, dislocation, incisional drainage, trochanteric bursitis, hematoma, DVT/PE, deep infection $\leq$ 6 weeks, superficial infection, and revisions (partial or complete) were the most frequently reported adverse events in the ceramic-ceramic group. The rates of these adverse events, when directly compared to the rate in the control group, did not demonstrate a statistically significant difference.

In the RNIA cohort, 54 C/C patients had a total of 95 postoperative systemic adverse events during the discharge interval through the post 2 year interval. 52 control patients had a total of 83 postoperative systemic adverse events. The most common systemic adverse events observed in both groups were related to the skeletal system. Nineteen of 146 (13%) patients reported 26 events and 22/130 (17%) patients reported 25 events related to the skeletal system in the C/C and C/P groups, respectively.

In the RNIA cohort, the other most frequently reported postoperative systemic adverse events in C/C patients were related to circulatory, digestive, integumentary, nervous, cardiac, muscular, or urinary systems. Rates of these and falls, anemia, deaths, DVT, PE, and surgery of the involved hip (but not affecting the implant) occurred with a frequency of between 1.4% (2/146 patients) and 6.2% (9/146 patients). DVT, PE occurred with greater frequency in the investigational group (2 patients) but none were reported in the control group. Intraoperatively, one incidence of hypoxia occurred in a bilaterally implanted C/C patient, and one incidence of hypotension occurred in a C/P patient.

In the RNIA cohort, the systemic postoperative adverse events in the C/C patients included allergic reaction, motor vehicle accident, pneumonia, electrolyte, hepatobiliary, renal, or respiratory abnormalities which occurred at a rate of 0.7% (each event reported once in 146 patients).

In the RNIA cohort, the operative site postoperative adverse events in the C/C hips included audible squeak in the hip, pelvic fracture, delayed wound healing, heterotopic ossification grade IV, I&D local, femoral head fracture, acetabular liner fracture, loosened stem, insufficient bone stock, head migration, and head subluxation which occurred at a rate of 0.6% (each event reported once in 174 hips). The majority of these appear to be device- or procedure-related.

Deaths

There were 6 deaths during the course of this study; 5 in the C/C group and one in the C/P group. All were in the RNIA cohort. One patient who died was a protocol deviation that is not reflected in Table 2 - Hip Accounting. Three of these patients in the C/C group died at, or prior to, the 1 year follow-up: one within the 18 days post operatively, and one 4 months post operatively, one at one year postoperatively. Two patients, died at the time of the 2 year or greater follow-up. In the C/P group, the patient died at the 2 year postoperative time point. Three patients' deaths (house fire death, 2 deaths due to lung cancer) in the C/C group and the one C/P group patient (heart disease) are clearly not related to the procedure or the device. The remaining 2 deaths occurred close to the surgical procedures associated with confirmed or suspected sepsis after revision or dislocation events.

Operative Site and systemic adverse events as well as revisions occurring in RNIA population are provided in time course adverse event distribution Tables **9-13** provided at the end of this document.

Summary of Safety

Patients in the REFLECTION ceramic group experienced more adverse events associated with the implant or procedure than the control group did, however this difference was not statistically significant.

There are different adverse events associated with the ceramic couple specifically liner fractures. The reasons for revision are similar with that anticipated of any total hip prosthesis (dislocation, infection, bone loss, component loosening/migration) except for intraoperative chipping of the ceramic liner that required cup/liner exchange and postoperative ceramic component fractures requiring revision. In this study, a higher incidence of heterotopic ossification was observed.

Treatment Results

For the RNIA cohort, mean operative time and blood loss were similar. The majority of bilateral procedures in both groups were staged procedures although more patients in the investigational group had same day bilateral surgeries (24) than in the control group (8). A posterior lateral approach was the most common surgical approach to the hip. In the investigational group the left hip and in the control group the right hip was implanted more frequently. The Synergy hip stem was used in 120 investigational hips and 94 hips in the control group. The Spectron EF stem was used as part of the construct in 53 investigational hips and 46 control hips. Bone graft was not used in the majority of patients in either group. When bone graft was used, the acetabulum was the site grafted most in

both treatment groups. In the majority of procedures no cement was used to fix the components. When cement was used, the femur was cemented in 54 and 47 procedures in the investigational and control groups respectively.

## 2. Effectiveness Results

Success outcome is based on a three part composite at the two years interval, whereby the hip had not undergone revision, had Total Harris Hip Score greater than or equal to 80, and no radiographic failure due to unacceptable radiolucencies or component subsidence/migration. Radiographs were evaluated by an independent radiologist at 24 months only.

RNIA Cohort preoperative baseline effectiveness evaluations on the HHS, ROM, and SF-12 were similar between the two groups (Table 5).

**Table 5, Baseline Evaluations - RNIA Cohort**

| Baseline Evaluations | | |
|---|---|---|
| | **RNIA C/C** | **RNIA C/P** |
| Harris Hip Score (100 pts) | 44.6 | 43.8 |
| HHS Pain score ( 44 pts) | 13.5 | 13.6 |
| HHS Function score (47 pts) | 24.3 | 23.3 |
| ROM Flexion (degrees) | 86.3 | 84.2 |
| SF-12 PCS | 29.5 | 28.7 |
| SF-12 MCS | 52.2 | 51.6 |

Table 6 provides a summary of Success Outcome for the two study groups (per protocol analysis).

**Table 6, Effectiveness Results and Success Criteria at Two Years Per Protocol[1]**

| Category | 2-year results | | | | | | 1-year results |
|---|---|---|---|---|---|---|---|
| | RNIA | | RIA | | RR | | CAC |
| | C/C | C/P | C/C | C/P | C/C | C/P | C/C |
| Enrolled * | 174 | 141 | 17 | 13 | 5 | 7 | 103 |
| Evaluated [A] | 126 | 85 | 12 | 6 | 2 | 1 | 53 |
| Mean Harris Hip Score (Total 100) | 96.0 (n=126) | 92.6 (n=85) | 92.8 (n=12) | 88.3 (n=6) | 98.5 (n=2) | 71.0 (n=1) | 95.3 (n=53) |
| Revision Success (hip not revised) | 122/126 (96.8%) | 84/85 (98.8%) | 11/12 (91.7%) | 6/6 (100%) | 2/2 (100%) | 1/1 (100%) | 49/53 (92.4%) |
| Harris Hip Success ( ≥ 80) | 121/126 (96.0%) | 76/85 (89.4%) | 11/12 (91.7%) | 5/6 (83.3%) | 2/2 (100%) | 0/1 (0%) | 49/53 (92.5%) |
| Radiographic Success [B] | 118/118 (100%) | 77/78 (98.7%) | 12/12 (100%) | 6/6 (100%) | 2/2 (100%) | 1/1 (100%) | 50/50 (100%) |
| Overall Success [C] | 113/122 (92.6%) | 70/81 (86.4%) | 11/13 (84.6%) | 5/6 (83.3%) | 2/2 (100%) | 0/1 (0%) | 46/54 (85.2%) |

[1] Per protocol patients evaluated at 24 months

* Enrolled is the number of hips implanted in the study by cohort.

[A] The number of evaluated, non-revised hips with an actual Total Harris Hip Score obtained at the 2 years follow-up. Partial evaluations not included in table.

[B] Denominator is the number of actual independent-read radiographs and not the number with any evaluations.

[C] Denominator is number of failures plus the number of hips with independent-read radiographs that were judged a success in the per-protocol population at 24 months.

The study device group (C/C) was demonstrated to be at least as good as the control (C/P) with respect to the success rate among all hips with complete data regardless of whether or not there was a protocol deviation at 2 years (C/P: 85/102=83.3% (141 – 39 hip exclusions) vs. C/C: 123/134=91.8% (174 – 40 hip exclusions) and the upper bound of one-sided 95% CI for the difference was less than 10%). Sensitivity analyses (e.g., last observation carry forward) including all the randomized hips showed that the missing data at 2 years did not change the conclusion that the REFLECTION Ceramic device (C/C) was not inferior to the control.

Results of multivariate regression analyses (logistic regression model and GEE model) justified the pooling across centers, hip replacement (bilateral/unilateral) and femoral stem cement use (yes/no). There was no statistically significant effect of age, gender or body mass index on the success outcome at 2 years. The adjusted odds ratio of success for C/C compared to C/P based on the logistic regression model (hips with missing data at 2 years were excluded) was 1.8 (95% CI: 0.8-4.3).

The overall success outcome reported in Table 6 incorporates elements of effectiveness. Other clinical measurements of clinical effectiveness are summarized in Table 7 for the RNIA cohort.

**Table 7, Time Course Effectiveness and SF-12 Health Survey Physical Scale - all Hips (RNIA)**

| | Preop | | 3 Months | | 6 Months | | 12 Months | | 24 Months | |
|---|---|---|---|---|---|---|---|---|---|---|
| | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P |
| N | 174 | 141 | 157 | 127 | 151 | 120 | 144 | 115 | 139 | 106 |
| Total Harris Hip Score Mean [1] (SD) | 44.6 (10.7) | 43.8 (9.7) | 84.2 (14.4) | 86.2 (13.6) | 90.8 (13.1) | 92.1 (10.6) | 93.9 (9.0) | 92.9 (10.8) | 95.6 (7.5) | 92.1 (10.5) |
| Total Harris Hip Pain Subscore Mean[2] (SD) | 13.5 (4.9) | 13.6 (5.0) | 37.7 (8.3) | 38.8 (7.9) | 39.8 (7.5) | 40.9 (6.2) | 41.0 (5.8) | 41.1 (6.2) | 42.2 (4.6) | 40.5 (6.5) |
| Total Harris Hip Function SubScore Mean[3] (SD) | 24.3 (7.6) | 23.3 (7.4) | 38.1 (7.9) | 38.9 (7.3) | 42.4 (6.5) | 42.4 (6.4) | 44.1 (5.0) | 43.1 (5.7) | 44.6 (4.5) | 42.8 (6.1) |
| Flexion (degrees) Range of Motion Mean (SD) | 86.3 (18.4) | 84.2 (22.3) | 102.2 (14.5) | 104.7 (13.5) | 109.0 (15.5) | 110.6 (15.8) | 109.9 (16.7) | 110.3 (16.2) | 111.8 (15.6) | 112.1 (16.6) |
| SF-12 Health Survey Physical Scale Score Mean[4] (SD) | 29.5 (7.5) | 28.7 (7.3) | 41.9 (9.9) | 41.9 (9.4) | 48.2 (9.4) | 47.9 (8.9) | 49.2 (9.0) | 48.3 (9.3) | 49.5 (8.6) | 47.1 (10.3) |

C/C=Ceramic-Ceramic group, C/P = Ceramic-Poly group
1 Total Harris Hip Score scale from 0 (worst) to 100 (best)
2 Harris Hip Pain Sub-Score scale from 0 (worst) to 44 (best)
3 Harris Hip Function Sub-Score scale from 0 (worst) to 47 (best)
4 The mean of the Physical Component Summary scale in the general U.S. population is 50±10

Clinical results in the RNIA cohort shows improvement in overall and subscore Harris hip scores indicating improvement in pain and function over the course of the study, with approximately 90% of the patients in the evaluated group with good to excellent results, with few radiographic failures, acceptable implant survival at 2 years comparable with the control and that in the conventional hip implant literature, and improved physical quality of life scores on the SF-12 health survey. Range of motion improved in both groups as compared to preoperative measurements, but were not statistically significant.
Overall success rates are no worse than the control.

## F. Clinical Results in Other Diagnostic Cohorts

The results presented in previous tables are specific to patients with a primary diagnosis of non-inflammatory arthritis of the involved hip. The clinical study also permitted enrollment of patients with inflammatory arthritis or patients requiring revision surgery for other hip devices that have failed. Patients were subject to the same inclusion/exclusion criteria and the same investigational plan as the RNIA cohort.

Summary of Inflammatory, Revision and Continued Access cohorts

Data was collected for patients with a diagnosis of inflammatory arthritis cohort (17 hips ) and revision of previously implanted hips (5 hips) The data from the inflammatory arthritis and revision cohorts is insufficient to make absolute

statements regarding safety and effectiveness in these diagnostic indications, however patients in both cohorts tended to have similar pain relief after surgery, and the patient outcomes in these populations showed a trend toward significant clinical benefit; relief of pain and return to function as measured by the Harris Hip Score, outweighing the risks of surgery in this population. Intraoperative (liner fractures, proximal linear femoral split fracture and postoperative events were similar to those of the primary osteoarthritis cohort including subsidence, migration, heterotopic ossification and revision (1 RIA).

In the Continued Access cohort, 5 revisions were reported in 103 hips (4.8%). These included 2 fractured liners during impaction which required revision of liner and cup. Three revisions occurred within 6 months. One hip had increased blood loss of 2300cc. Postoperative revision and loosening occurred in 5 patients.

Revisions for the Continued Access cohort are detailed in Table 8.

**Table 8, Hips Revised - Continued Access Cohort**

| Treatment | Interval | Reason for Revision | Components Revised |
|---|---|---|---|
| C/C | 3 month | prolonged dislocation/soft tissue laxity | Head |
| C/C | 6 month | recurrent posterior dislocations | Stem |
| C/C | 6 month | subsidence/loosening of stem | head, stem |
| C/C | 1 year | infection/loosened cup | cup, liner |
| C/C | 2 years | Osteolysis | head, stem |

C/C=ceramic-ceramic

Safety

As with the RNIA cohort, the preliminary safety data for the RIA, RR, and CAC cohorts indicate that there are certain adverse events associated with the brittle material and different implantation techniques as compared to the conventional hip systems. The data suggest there are specific patients who had less successful outcomes (less successful HHS) including those who were protocol deviations in this study, (e.g. weight above recommended BMI), and those with preoperative/intraoperative risk factors including noncemented components, male gender, prior surgery, prior ectopic bone, anterolateral surgical approach , complexity of surgery. These suggest that specific patient and intraoperative selection criteria be advised. The data related to the formation of Heterotopic ossification suggest a recommendation for prophylaxis in those conditions, even in primary hip arthroplasty.

Effectiveness

The absolute effectiveness data for the RIA cohort cannot be determined due to the small sample size; however preliminary data shows that the Reflection Ceramic Acetabular System device used in the treatment of inflammatory arthritis of the hip may improve the majority of patients' pain and function with improved physical quality of life as measured by the HHS, SF-12.

## PACKAGING AND LABELING

Implants should be accepted only if received by the hospital or surgeon with the factory packaging and labeling intact. If the sterile barrier has been broken, return the component to Smith & Nephew, Inc.

## STERILIZATION

Implant components are supplied sterile to a Sterility Assurance Level (SAL) of $10^{-6}$. Metal components are sterilized by a minimum of 25 kiloGrays of gamma irradiation. Alumina ceramic components are sterilized by ethylene oxide gas. All components are supplied in protective packaging and trays. Inspect packages for punctures or other damage prior to surgery. Instruments used to implant the device system are supplied non-sterile and must be sterilized prior to use using one of the following validated, recommended methods:

**CYCLE PARAMETERS**

- **Prevacuum Flash Cycle:** 4 pulses (Maximum = 26.0 psig (2.8 bars) & Minimum = 10.0 inHg (339 millibars)) with a minimum exposure time of 4 minutes at 270°F to 275°F (132°C to 135°C), followed by a 1 minute purge
- **High Temperature Gravity Cycle:** 270°F to 275°F (132°C to 135°C) with a minimum exposure time of 10 minutes, followed by a 1 minute purge and at least 15 minutes of vacuum drying.
- **Prevacuum Cycle:** 4 pulses (Maximum = 26.0 psig (2.8 bars) & Minimum = 10.0 inHg (339 millibars)) with a minimum exposure time of 4 minutes at 270°F to 275°F (132°C to 135°C), followed by a 1 minute purge and at least 15 minutes of vacuum drying.

## RESTERILIZATION

DO NOT RESTERILIZE REFLECTION Ceramic Acetabular System implant components. Porous coated metal implants and alumina ceramic implant components require special cleaning procedures. Contact your local Smith & Nephew, Inc. Sales Representative regarding procedures to return components.

**Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.**

**INFORMATION**

For further information, please contact Smith & Nephew, Inc. Customer Service at (800) 238-7538 for calls within the continental USA and (901) 396-2121 for all international calls.

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**Table 9, Time Course Distribution of Operative Site Adverse Events for Non-Inflammatory Arthritis (RNIA) Hips**

| Cohort | Ceramic-Ceramic Group 174 Hips | | | | | | | | Ceramic-Poly Group 141 Hips | | | | | | | | Continued Access Group 103 Hips | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Interval | IO | DC | 3M | 6M | 12M | 24M | 24+M | Tot | IO | DC | 3M | 6M | 12M | 24M | 24+M | Tot | IO | DC | 3M | 6M | 12M | 24M | 24+M | Tot |
| No. of Hips Evaluated | 174 | 174 | 158 | 151 | 144 | 139 | 5 | 74 | 141 | 141 | 127 | 120 | 115 | 106 | 3 | 141 | 103 | 103 | 87 | 82 | 61 | 1 | 0 | 103 |
| Total No. of Events | 21 | 12 | 38 | 18 | 12 | 23 | 3 | 27 | 8 | 13 | 24 | 10 | 7 | 12 | 3 | 77 | 8 | 1 | 8 | 3 | 2 | 0 | 0 | 22 |
| Audible Squeak | | | | | | | 1 | 1 | | | | | | | | | | | | | | | | |
| Blood Loss > 1500 ml | 6 | | | | | | | 6 | 2 | | | | | | | 2 | 1 | | | | | | | 1 |
| Bone Fracture: Femur | | | | | | | | | | | | | | 1 | | 1 | | | | | | | | |
| Bone Fracture: Pelvis | | | | | 1 | | | 1 | | | | | | | | | | | | | | | | |
| Cardiac Arrythmia | | | | | | | | | | | | | | | | | 1 | | | | | | | 1 |
| Deep Vein Thrombosis | | | 2 | | | | | 2 | | | | | | | | | | | | | | | | |
| Delayed Wound Healing | | 1 | | | | | | 1 | | | 1 | | | | | 1 | | | | | | | | |
| Difficulty Implanting Liner | 2 | | | | | | | 2 | | | | | | | | | 1 | | | | | | | 1 |
| Dislocation: Head | | | 7 | | | 2 | 1 | 10 | 1 | 4 | | | | 1 | 2 | 8 | | | 3 | 1 | | | | 4 |
| Fracture Liner | 3 | | | | | | | 3 | | | | | | | | | 2 | | | | | | | 2 |
| Hematoma | | | 3 | | | | | 3 | | | 1 | | | | | 1 | | | 1 | | | | | 1 |
| HO: Grade I | | 7 | 14 | 11 | 4 | 8 | | 44 | | 7 | 13 | 6 | 5 | 6 | | 37 | | | 1 | | | | | 1 |
| HO: Grade II | | | 1 | 2 | | 5 | | 8 | | | 1 | 2 | 1 | 1 | | 5 | | | | | | | | |
| HO: Grade III | | | 3 | 2 | 3 | 1 | | 9 | | | | | | 2 | | 2 | | | | | | | | |
| HO: Grade IV | | | | | | 1 | | 1 | | | | | | | | | | | | | | | | |
| I&D Local | | | 2 | | | | | 2 | | | 1 | | | | | 1 | | | | | | | | |
| I&D Non-Local | | | | | | | | | | | 1 | | | | | 1 | | | | | | | | |
| Implant Fracture Head | | | | | | 1 | | 1 | | | | | | | | | | | | | | | | |
| Implant Fracture: Liner | | | | | | 1 | | 1 | | | | | | | | | | | | | | | | |
| Implant Loosened: Cup | | | | | | | | | | | | | | | | | | | | 1 | | | | 1 |
| Implant Loosened: Stem | | | | | | | 1 | 1 | | | | 1 | | | | 1 | | | | 1 | | | | 1 |
| Incisional Drainage | | 3 | 3 | | | | | 6 | | 1 | 1 | | | | | 2 | | | 1 | | | | | 1 |
| Incisional Tenderness | | | | | | | | | | | | 1 | | | | 1 | | | | | | | | |
| Infection: Deep ≤ 6 WKS | | | 1 | | | 1 | | 2 | | | 1 | | | | | 1 | | | 1 | | | | | 1 |
| Infection: Deep > 6 WKS | | | | | | | | | | 1 | | | | | | 1 | | | | | 1 | | | 1 |
| Infection: Superficial | | 1 | 1 | | | | | 2 | | | 3 | | | | | 3 | | | | | | | | |
| Insufficient Bone Stock | 1 | | | 1 | | | | 2 | | | | | | | | | | | | | | | | |
| Migration: Head | | | | | | 1 | | 1 | | | | | | | | | | | | | | | | |
| Nerve Injury | 1 | | | | | | | 1 | | | | | | | | | | 1 | | | | | | 1 |

| | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Osteolysis | | | | | | | | | | | | | | | | | | | | | 1 | | | 1 |
| Proximal Femur Fracture | 7 | | | | | | | 7 | 4 | | | | | | | 4 | 3 | | | | | | | 3 |
| Pulmonary Embolism | | | | | 2 | | | 2 | | | | | | | | | | | | | | | | |
| Reoperation (Not A Revision) | | | 1 | 1 | | | | 2 | | | | | | | | | | | | | | | | |
| Subluxed / Subside Head | | | | | 1 | | | 1 | | | | | | 1 | | 1 | | | | | | | | |
| Subluxed / Subside Stem | | | | | | | | | | | | | | | | | | | 1 | | | | | 1 |
| Trochanteric Bursitis | | | | 1 | 1 | 2 | | 4 | | | 1 | | 1 | | 1 | 3 | | | | | | | | |
| Trochanteric Fracture | 1 | | | | | | | 1 | 1 | | | | | | | 1 | | | | | | | | |

IO=intraoperative; DC=discharge; 3M= 3 months; 6M= 6 months; 12M= 12 months; 24M= 24 months; 24+M= post 24 months. Excludes adverse events after the first revision of a C/C or C/P device.

Revisions are considered Operative Site events, and RNIA revisions are reported separately in Table 3 and listed in time course as Table 11.

**Table 10, Time Course Distribution of Systemic Adverse Events for Non-Inflammatory Arthritis (RNIA) Subjects**

| Cohort | Ceramic-Ceramic Group 146 Subjects | | | | | | | | Ceramic-Poly Group 130 Subjects | | | | | | | | Continued Access Group 88 Subjects | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Interval | IO | DC | 3M | 6M | 12M | 24M | 24+M | Tot | IO | DC | 3M | 6M | 12M | 24M | 24+M | Tot | IO | DC | 3M | 6M | 12M | 24M | 24+M | Tot |
| No. of Hips Evaluated | 146 | 146 | 133 | 125 | 122 | 119 | 4 | 146 | 130 | 130 | 118 | 114 | 108 | 98 | 3 | 130 | 88 | 88 | 74 | 69 | 54 | 1 | 0 | 88 |
| Total No. of Events | 1 | 24 | 29 | 10 | 12 | 14 | 6 | 96 | 1 | 19 | 15 | 6 | 7 | 23 | 13 | 84 | 0 | 9 | 7 | 2 | 6 | 2 | 0 | 26 |
| Allergic Reaction | | | 1 | | | | | 1 | | 1 | | | | | | 1 | | | | | | | | |
| Anemia | | 3 | 2 | | | | | 5 | | 2 | | | | | | 2 | | | | | | | | |
| Death | | | 1 | | | 1 | 1 | 3 | | | | | | 1 | | 1 | | | | | | | | |
| Dislocation Non-Operative Hip | | | | | | | | | | | | | | 1 | | 1 | | | | | | | | |
| Fall | | 1 | 1 | 2 | | 1 | | 5 | | | 1 | 1 | 1 | 4 | | 7 | | | | | | | | |
| Fever | | 3 | 3 | | | | | 6 | | 1 | 2 | | | | | 3 | | | 1 | | | | | 1 |
| Hernia | | | | | | | | | | | | 1 | | | | 1 | | | | | | | | |
| Hypotension | | | | | | | | | 1 | | | | | | | 1 | | | | | | | | |
| Hypoxia | 1 | | | | | | | 1 | | | | | | | | | | | | | | | | |
| Motor Vehicle Accident | | | | 1 | | | | 1 | | | | | | 1 | | 1 | | | | | | | | |
| Pneumonia | | | 1 | | | | | 1 | | | | | | | | | | | | | | | | |
| Surgery (unrelated To Study Hip) | | | 1 | | | | 1 | 2 | | | 1 | | 1 | | 4 | 6 | | | | | | | | |
| Systemic: Cardiac | | 1 | 2 | | | | | 3 | | 5 | 2 | | | | | 7 | | | | | | | | |
| Systemic: Circulatory | | 2 | 4 | | 1 | 1 | | 8 | | 1 | 3 | 1 | | 1 | | 6 | | 3 | 1 | | 1 | | | 5 |
| Systemic: Digestive | | 7 | 2 | | 1 | | | 10 | | 5 | | | | 1 | | 6 | | 2 | 1 | | | | | 3 |
| Systemic: Genetic Disorder | | | | | | | | | | | | | | | | | | | 1 | | | | | 1 |
| Systemic: Fluid and Electrolyte | | 1 | | | | | | 1 | | 1 | | | | | | 1 | | | | | | | | |
| Systemic: Hepatobiliary | | | 1 | | | | | 1 | | | | | | | | | | | | | | | | |
| Systemic: Infection (unrelated to surgical wound) | | | | | | | | | | | | | | | | | | 1 | | | | | | 1 |
| Systemic: Integumentary | | 3 | 1 | | 2 | 1 | | 6 | | 1 | | | 1 | | 1 | 3 | | 1 | | | | | | 1 |
| Systemic: Muscular | | 1 | 2 | | | | | 3 | | | | | | 1 | | 1 | | 1 | | | 1 | | | 2 |
| Systemic: Nervous | | 1 | 1 | 3 | 2 | 2 | | 9 | | | | | | 3 | | 3 | | | | | | | | |
| Systemic: Renal | | | 1 | | | | | 1 | | | 1 | | | | 1 | 2 | | | 1 | | | | | 1 |
| Systemic: Reproductive | | | | | | | | | | | | | | | 1 | 1 | | | | | 1 | | | 1 |
| Systemic: Respiratory | | | | | | 1 | | 1 | | | 1 | | | 1 | | 2 | | | 1 | | | | | 1 |
| Systemic: Skeletal | | 1 | 4 | 4 | 6 | 7 | 4 | 26 | | | 4 | 2 | 4 | 9 | 6 | 25 | | | 1 | 2 | 3 | 2 | | 8 |
| Systemic: Urinary | | | 1 | | | 1 | | 2 | | 2 | | 1 | | | | 3 | | 1 | | | | | | 1 |

IO=intraoperative; DC=discharge; 3M= 3 months; 6M= 6 months; 12M= 12 months; 24M= 24 months; 24+M= post 24 months.
Excludes adverse events after the first revision of a C/C or C/P device.

## Table 11, Time Course of Hip Revisions - RNIA Cohort

| Revised | Number of Hips by Interval | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | IO | | DC | | 3M | | 6M | | 12M | | 24M | | 24+M | | Total | |
| | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P |
| No. of Revisions † | 2 | 1 | | 1 | 2 | 1 | 1 | | | | 1 | | 2 | | 8 | 3 |
| Cup | 2 | | | | 1 | 1 | 1 | | | | | | 1 | | 5 | 1 |
| Liner | 2 | 1 | | 1 | 2 | 1 | 1 | | | | 1 | | 1 | | 7 | 3 |
| Head | | | | 1 | 2 | 1 | 1 | | | | 1 | | 2 | | 6 | 2 |
| Stem | | | | | 1 | 1 | | | | | | | 1 | | 2 | 1 |

Intervals: IO=Intraoperative; DC=Discharge; 3M=3 months; 6M=6 months; 12M=12 months; 24M=24 months; 24+M=post-24 months

† Number of revisions for any primary component implanted. The numbers on subsequent rows for each identified implant component denote number of primary implants revised, i.e. in the "IO" interval 2 cups and 2 liners were revised in two separate hip revisions. "Total" columns for each group summarize the number of revision events and number of components revised.

Two (2) intraoperative revisions in C/C hips were due to chipping of ceramic liners during placement that required cup and liner exchange. One (1) intraoperative revision in C/P hip was due to instability. Postoperatively, in the RNIA cohort, the reasons for revision in C/C device hips were dislocation (1 at 3M, 1 at 6M), infection (3M), head fracture (24M), liner fracture (24+M) and loose stem (24+M). In the C/P device hips, the reasons for revision were instability (1 at IO, 1 at DC) and infection (3M).

## Table 12, Time Course of Hip Revisions - CAC Cohort

| Revised | Number of Hips by Interval | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | IO | | DC | | 3M | | 6M | | 12M | | 24M | | 24+M | | Total | |
| | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P |
| No. of Revisions † | 2 | | | | 1 | | 2 | | 1 | | 1 | | | | 7 | |
| Cup | 2 | | | | | | | | 1 | | | | | | 3 | |
| Liner | 2 | | | | | | | | 1 | | | | | | 3 | |
| Head | | | | | 1 | | 1 | | | | 1 | | | | 3 | |
| Stem | | | | | | | 2 | | | | 1 | | | | 3 | |

Intervals: IO=Intraoperative; DC=Discharge; 3M=3 months; 6M=6 months; 12M=12 months; 24M=24 months; 24+M=post-24 months. CAC cohort had only ceramic/ceramic implants.

† Number of revisions for any primary component implanted.

Two (2) intraoperative revisions in C/C hips were due to chipping of ceramic liners during placement that required cup and liner exchange. Postoperatively in the CAC cohort, the reasons for revision in C/C device hips were dislocation (1 at 3M, 1 at 6M), loose stem (6M), infection/loose cup (24M), and osteolysis (24M).

## Table 13, Time Course of Hip Revisions - RIA Cohort

| Revised | Number of Hips by Interval | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | IO | | DC | | 3M | | 6M | | 12M | | 24M | | 24+M | | Total | |
| | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P | C/C | C/P |
| No. of Revisions † | | | | | | | 1 | | | | | | | | 1 | |
| Cup | | | | | | | | | | | | | | | | |
| Liner | | | | | | | | | | | | | | | | |
| Head | | | | | | | 1 | | | | | | | | 1 | |
| Stem | | | | | | | 1 | | | | | | | | 1 | |

Intervals: IO=Intraoperative; DC=Discharge; 3M=3 months; 6M=6 months; 12M=12 months; 24M=24 months; 24+M=post-24 months. CAC cohort had only ceramic/ceramic implants enrolled.

† Number of revisions for any primary component implanted.

In the RIA cohort, the reason for revision in the C/C device hip was stem subsidence at 6M.